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Original Research

Incidence of hemorrhagical manifestations in cerebral malaria patients

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***ABSTRACT*:**
Background: Cerebral malaria is the most severe neurological complication of infection with Plasmodium falciparum malaria. It is a clinical syndrome characterized by coma and asexual forms of the parasite on peripheral blood smears. Mortality is high and some surviving patients sustain brain injury which manifest as long-term neuro-cognitive impairments. The mechanisms of neural injury in cerebral malaria are poorly understood. Although the pathogenesis of cerebral malaria is also incompletely understood, an insight into it can provide leads to the mechanisms of brain injury. **Aim of the study:** To evaluate the incidence of hemorrhagical manifestations in cerebral malaria patients. **Materials and methods:** The study was conducted in the Department of General Medicine of the Medical institute. For the study, 60 patients admitted to the medical ward with symptoms of cerebral malaria were included in our study. Patients below 12 years, pregnant women, patients unfit for MRI and those having other systemic conditions such as diabetes, leukemia were excluded from the study. After obtaining an informed consent, all patients were subjected to a preoperative work up. Majority of patients had brief episodes of loss of consciousness and few episodes of focal seizures that responded to anticonvulsants. All the patients were subjected to anti-malarial treatment along with supportive treatment. **Results:** A total of 60 patients were included in the study. The number of male patients in the study was 34 and number of female patients was 26. The mean age of the patients was 35.72 years. In total 20 patients were diagnosed from the MRI having cerebral hemorrhagic infarct. The basal ganglia infarct was seen in 5 patients, thalamus infarct in 6 patients, cerebellum infarct in 3 patients, pontine infarct in one patient, parietal occipital lobe infarct in 4 patients and other findings were seen in 1 patient. **Conclusion**: Within the limitations of the study we conclude that patients with cerebral malaria are at high risk for cerebral hemorrhage and MRI should be conducted for each patient for diagnosis at early stage.
Keywords: Cerebral malaria, cerebral infarct, MRI brain

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INTRODUCTION:

Cerebral malaria is the most severe neurological complication of infection with Plasmodium falciparum malaria. It is a clinical syndrome characterized by coma and asexual forms of the parasite on peripheral blood smears. Mortality is high and some surviving patients sustain brain injury which manifest as long-term neuro-cognitive impairments. [1] The World Health Organization defines cerebral malaria as a clinical syndrome characterized by coma at least 1 hour after termination of a seizure or correction of hypoglycemia, asexual forms of Plasmodium falciparum parasites on peripheral blood smears and no other cause to explain the coma. [2] In practice, this definition is non-specific. Patients in whom coma is caused by other encephalopathies (e.g. viral encephalitis, poisoning and metabolic disease) or previously unrecognized neurological abnormalities but have incidental parasitemia (a common phenomenon in malaria endemic areas) may be included. Thus, in a postmortem study of Malawian children dying with a clinical diagnosis of cerebral malaria, 24% had other causes of death. [3] This lack of specificity is problematic

for clinical and pathogenesis studies. The increased specificity accorded by recent descriptions of retinal changes in cerebral malaria is should address this issue. [4] The mechanisms of neural injury in cerebral malaria are poorly understood. Although the pathogenesis of cerebral malaria is also incompletely understood, an insight into it can provide leads to the mechanisms of brain injury. In addition, descriptions of the prognostic factors for neuro-cognitive sequelae and post-mortem studies have provided some understanding. Three observations however raise questions; 1) how does a largely intravascular parasite cause so much neuronal dysfunction? 2) despite the large number of parasites in the brain of most patients, why is coma so rapidly reversible with treatment and with very little demonstrable tissue necrosis? 3) Despite similar presentation, why do some children have a poor neurological outcome while others improve with hardly any deficits? [5, 6] Hence, the present study was conducted to evaluate the incidence of hemorrhagical manifestations in cerebral malaria patients.

MATERIALS AND METHODS:

The study was conducted in the Department of General Medicine of the Medical institute. The ethical clearance for the study was obtained from the ethical board of the institute prior to commencement of the study. For the study, 60 patients admitted to the medical ward with symptoms of cerebral malaria were included in our study. Patients below 12 years, pregnant women, patients unfit for MRI and those having other systemic conditions such as diabetes, leukemia were excluded from the study. After obtaining an informed consent, all patients were subjected to a preoperative work up. The patients included in the study had symptoms like fever with chills and rigors for the more than 7 days. Their liver function and renal function tests were deranged and the peripheral smear was positive for malarial parasites. Majority of patients had brief episodes of loss of consciousness and few episodes of focal seizures that responded to anticonvulsants. All the patients were subjected to anti-malarial treatment along with supportive treatment. The treatment provided included administration of intravenous quinine dihydrochloride, intravenous fluids, antipyretics, and anti-inflammatory drugs. For the evaluation of cerebral hemorrhage patients were subjected to MRI. The findings of the MRI were recorded and subjected to statistical analysis.

The statistical analysis of the data was done using SPSS version 11.0 for windows. Chi-square and Student's t-test were used for checking the significance of the data. A p-value of 0.05 and lesser was defined to be statistically significant.

RESULTS:

Table 1 shows demographic data of the patients. A total of 60 patients were included in the study. The number of male patients in the study was 34 and number of female patients was 26. The mean age of the patients was 35.72 years. **[Fig 1]** Table 2 shows the pattern of hemorrhagical manifestations in cerebral malaria patients. In total 20 patients were diagnosed from the MRI having cerebral hemorrhagic infarct. The basal ganglia infarct was seen in 5 patients, thalamus infarct in 6 patients, cerebellum infarct in 3 patients, pontine infarct in one patient, parietal occipital lobe infarct in 4 patients and other findings were seen in 1 patient. The results were compared and found to be statistically significant. ($p<0.05$)

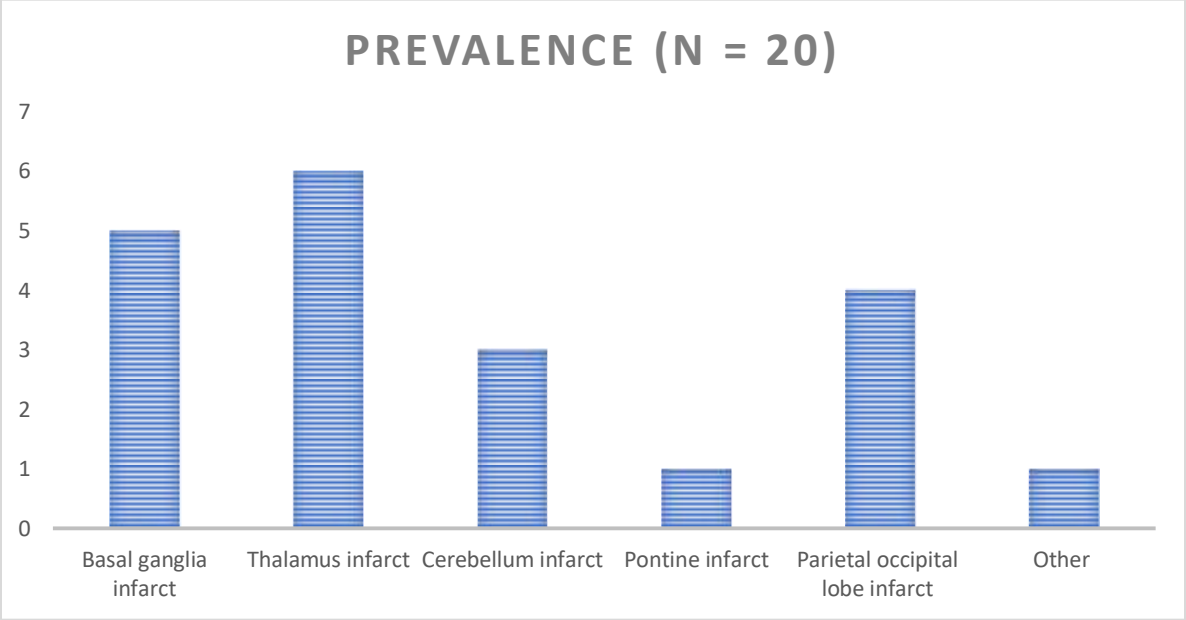
Table 1: Demographic data of the patients

Variables	Frequency
Total no. of patients	60
No. of male patients	34
No. of female patients	26
Mean age of the patients (years)	35.72

Table 2: Pattern of hemorrhagical manifestations in cerebral malaria patients

Area of Hemorrhagic infarct	Prevalence (N = 20)	P value
Basal ganglia infarct	5	0.002
Thalamus infarct	6	
Cerebellum infarct	3	
Pontine infarct	1	
Parietal occipital lobe infarct	4	
Other	1	
Total	20	

Fig 1:



DISCUSSION:

In the present study, we observed that a total of 60 patients were included in the study. The mean age of the included patients was 35.72 years. Cerebral infarct was seen in 20 patients. Basal ganglia infarct was also commonly seen. The results were statistically significant. The results were compared with previous studies and were found to be consistent. Carter JA et al investigated the long-term developmental outcome of CM and malaria with complicated seizures (M/S). They followed up a cohort of children previously exposed to CM or M/S and children unexposed to either condition. All children between 6 and 9 years of age, exposed to CM, and an equal number of children exposed to M/S were identified from databases of hospital admissions from 1991 to 1998. The unexposed group was randomly selected from a census database. The children's performance was measured using assessments of cognition, motor, speech and language, hearing and vision. A parental questionnaire was used to identify children with epilepsy. CM group scores were significantly lower than unexposed group scores on the assessments of higher level language, vocabulary, pragmatics and non-verbal functioning. The areas of significantly reduced functioning for the M/S group were concentrated on phonology, pragmatics and behaviour. The performance of the active epilepsy group was significantly poorer than that of the group without epilepsy on the tests of comprehension, syntax, pragmatics, word finding, memory, attention, behaviour and motor skills. They concluded that CM and M/S are associated with developmental impairments. If these impairments persist, this may have implications for least 250,000 children in Sub-Saharan Africa each year. Idro R et al determined risk factors for impairments following cerebral malaria by examining hospital records of 143 children aged 6-9 years, previously admitted with cerebral malaria, who were assessed at least 20 months after discharge to detect motor, speech and language, and other cognitive (memory, attention, and non-verbal functioning) impairments. The median age on admission was 30 months (IQR 19-42) and the median time from discharge to assessment was 64 months (IQR 40-78). Thirty four children (23.8%) were defined as having impairments: 14 (9.8%) in motor, 16 (11.2%) in speech and language, and 20 (14.0%) in other cognitive functions. Previous seizures, deep coma on admission, focal neurological signs observed during admission, and neurological deficits on discharge were independently associated with persisting impairments. In addition, multiple seizures were associated with motor impairment, age <3 years, severe malnutrition, features of intracranial hypertension, and hypoglycaemia with language impairments, while prolonged coma, severe malnutrition, and hypoglycaemia were associated with impairments in other cognitive functions. They concluded that risk factors for persisting neurological and cognitive impairments following cerebral malaria include multiple seizures, deep/prolonged coma, hypoglycaemia, and clinical features of intracranial hypertension. Although there are overlaps in impaired functions and risk factors, the differences in risk factors for specific functions may suggest separate mechanisms for neuronal damage. These factors could form the basis of future preventive, strategies for persisting impairments. [7, 8]

Oluwayemi IO et al performed a prospective study describing persisting neurological impairments post discharge among children treated for cerebral malaria. In addition the study was designed to investigate the frequency of persistent neurologic deficits and the risk factors for their persistence in these patients. The case records of 160 patients treated for CM at the Paediatrics Department of University College Hospital, Ibadan from January 2004 to November 2006 were reviewed to recruit cases. Recruited survivors were then followed up for information concerning the presence and persistence of neurological sequelae. A total of 160 children aged 9 months to 134 months were admitted and treated for CM during the study period. One hundred and thirty one (81.9%) survived while 29 (18.1%) died. The 131 survivors of cerebral malaria consisted of 64 boys and 67 girls. Neurological sequelae occurred in 13.7% of survivors of cerebral malaria at discharge and 4.6% at follow up. Six children with neurological deficits at discharge had persistence of deficits 6 months post-hospital discharge and one at 24 months. No associations were found between hypoglycemia, anemia, age, sex and multiplicity of convulsions, and persistence of neurologic sequelae. The persisting neurologic deficits among survivors at follow up were: memory impairment (1.5%), seizure disorders (0.8%), visual impairment (0.8%), speech impairment (0.8%), monoparesis (0.8%) and hyperactivity (0.8%) at follow up. The longest persisting sequelae lasted for at least 24 months. They concluded that neurologic deficits are not uncommon complications of CM. Neurologic sequelae may persist for as long as 24 months or more in survivors of childhood CM. There is no association between the risk factors for neurologic deficits and persistent neurologic sequelae. Brim R et al assessed the relationship between magnetic resonance imaging (MRI) findings and long-term outcomes. They reported baseline characteristics of the cohort and outcomes at 1 month. At enrollment, CM cases were more likely to come from families with fewer socioeconomic resources and to have health characteristics that increase risk for malaria. In children younger than 5 years, cases were delayed in motor, language, and social development by approximately 6 months, compared with controls. More significant delays occurred in those with MRI abnormalities at the 1-month follow-up visit. There were no differences between cases and controls in inhibitory self-control, nor in cognitive function in children ≥ 5 years of age. The latter finding may be related to the smaller sample size, case-control imbalance in socioeconomic status, or the use of cognitive and behavioral assessments that are less culturally appropriate to this population. [9, 10]

CONCLUSION:

Within the limitations of the study we conclude that patients with cerebral malaria are at high risk for cerebral hemorrhage and MRI should be conducted for each patient for diagnosis at early stage.

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